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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/535,140	05/17/2005	Christelle Marie Guittet	05-367	3587

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EXAMINER	
AZARIAN, SEYED H	

ART UNIT	PAPER NUMBER
2624	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/535,140	GUITTET ET AL.	
	Examiner	Art Unit	
	Seyed Azarian	2624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-9,11-22,24-30 and 32-34* is/are allowed.

6)☒ Claim(s) *10,23 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 May 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/24/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO AMENDMENT

1. Applicants' arguments filed, 9/24/2008, see page 13 through page 16, of remark, with respect to cancellation of claim 4, and amended claims 10, 11, 14, 23, 24, 27, 28, 29, 30, 31, 32, 33 and 34, have been fully considered but they are moot in view of the new ground (s) of rejection as necessitated by applicant's amendment is made in view of Sundbland et al (The use of Image analysis and automation for measuring mitotic index in apical conifer meristems).

However in brief telephone interview, examiner suggested ways to clarify the independent claim or amend the claim that may overcome the prior art of record, but agreement was not reached.

Applicant argues in essence that regarding claim 10" that Vaisberg does not discloses "color image data, but instead monochromatic image data".

The applicant is respectfully reminded that, it is noted that the features upon which applicant relies, "color image data" are not recited in the rejected claim 10.

Applicant argues in essence that regarding claim 10" that Vaisberg does not discloses use histopathological (diseased tissue) specimen image data

Contrary to the applicant's assertion, limitations in the amended claim, Examiner indicates that Vaisberg disclose (Fig. 14A-14G, page 29 and 30, refer to human lung cancer).

Applicant argues in essence regarding claim 10 that Vaisberg does not disclose "a threshold to discriminate between mitotic and non-mitotic". Examiner indicates that Vaisberg discloses (page 12, threshold algorithms and threshold values is chosen to discriminate between cell, also page 11, lines 10-24, refer to stains).

However, for this feature "limitations in the amended claim", Examiner using this reference supplied with this action Sundbland et al (The use of Image analysis and automation for measuring mitotic index in apical conifer meristems), discloses page 1750, after staining, the apical meristem was removed from each bud and placed in a drop of 45% acetic acid on a microscope slide. Squashing was made by gently applying a coverslip over the sample and finally applying pressure to the coverslip, thus squashing the hydrolysed meristem into a single cell layer preparation. Further page 1752, statistical analysis PCA was first used to obtain an overview of differences and similarities between different cell cycle stages in terms of image analysis parameters. Thereafter, PCA was used to construct a model based only on interphase nuclei, and used to differentiate between dividing and non-dividing cells..For all multivariate studies, 14 image analysis parameters were used. To minimize problems related to variations in illumination of samples under the microscope or variations in staining intensity, all parameters except for Area--Fract, were relative parameters, calculated from original image parameters according to Table 1. For PCA, the systematic variation in the data matrix x composed of the variables (i.e. image parameters) and objects (i.e. nuclei) was described by the model).

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify Vaisberg invention according to the teaching of Sundbland because combination of Vaisberg classifying cells based on information in cell images and Sundbland staining procedure provides improve of measurement of mitotic activity, which can easily be implemented in an imaging device.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 10, 23 and 31, are rejected under 35 U.S.C. 103(a) as being unpatentable over Vaisberg Eu (WO 02/47032) in view of Sundbland et al (The use of Image analysis and automation for measuring mitotic index in apical conifer meristems).

Regarding claim 10, Vaisberg discloses a method of measuring mitotic activity from histopathological specimen image data, the method having the steps of (page 3, lines 7-8, analyze images of cells and categorize the cells in particular cell cycle phases based upon certain features);

a) measuring an intensity profile of an image region corresponding to a potentially mitotic figure (page 3, lines 9-27, characterize a cell as mitotic based on morphological and textual parameter such as pixel intensities);

b) counting the image region as indicating a mitotic figure if its profile has a value greater than a prearranged threshold at a position in the profile having intensity associated with mitotic figure imagery (page 12, lines 1-9, pixels with intensity values above threshold in a given neighborhood are belong to a particular cell).

However Vaisberg does not explicitly state its corresponding "staining a histopathological specimen with a staining agent to delineate tissue and cellular structure appropriately for assessment of mitotic activity". On the other hand, Sundbland discloses page 1750, after

staining, the apical meristem was removed from each bud and placed in a drop of 45% acetic acid on a microscope slide. Squashing was made by gently applying a coverslip over the sample and finally applying pressure to the coverslip, thus squashing the hydrolysed meristem into a single cell layer preparation. Further page 1752, statistical analysis PCA was first used to obtain an overview of differences and similarities between different cell cycle stages in terms of image analysis parameters. Thereafter, PCA was used to construct a model based only on interphase nuclei, and used to differentiate between dividing and non-dividing cells..For all multivariate studies, 14 image analysis parameters were used. To minimize problems related to variations in illumination of samples under the microscope or variations in staining intensity, all parameters except for Area--Fract, were relative parameters, calculated from original image parameters according to Table 1. For PCA, the systematic variation in the data matrix x composed of the variables (i.e. image parameters) and objects (i.e. nuclei) was described by the model).

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify Vaisberg invention according to the teaching of Sundbland because combination of Vaisberg classifying cells based on information in cell images and Sundbland staining procedure provides improve of measurement of mitotic activity, which can easily be implemented in an imaging device.

With regard to claims 23 and 31 the arguments analogous to those presented above for claim 10 are respectively applicable to claims 23 and 31.

REASONS FOR ALLOWABLE CLAIMS

4. The following is an examiner's statement of reasons for allowance.

Claims 1-9, 11, 17-22, 24 and 32 are allowable.

The instant invention generally relates to a method, an apparatus and a computer program for measurement of mitotic activity, which indicates cell division taking place in a tissue specimen: it is particularly relevant to making measurements on potentially cancerous tissue such as breast cancer tissue. The method is also relevant to other forms of cancer such as colon and cervical cancer.

Claim 1, representing claim 17, the closest prior art of record (Vaisberg) references do not disclose or suggest, among other things, "selecting from among the identified pixels a reference pixel which is sufficiently close in position and luminance to another identified pixel to provide a reference colour, locating pixels in the image data with luminance's sufficiently close to that of the reference colour to indicate potentially mitotic figures, incrementing image regions corresponding to potentially mitotic figures from the located pixels by adding pixels thereto, potential increments to image regions being implemented or rejected by according to whether or not their luminance's are sufficiently close to respective image region luminance's and sufficiently far from an image data background luminance, and selecting grown image regions on the basis of thresholds for image region area, compactness and width/height ratio, counting selected grown image regions as actually indicating mitotic figures on the basis of a threshold for number of such regions".

Additionally claim 11 representative of claims 24 and 32, the closest prior art of record (Vaisberg and Sundbland) does not teach or suggest, among other things, "computer apparatus for measuring mitotic activity from histopathological specimen image data obtained from a histopathological specimen stained with a staining agent to delineate tissue and cellular structure

appropriately for assessment of mitotic activity, the apparatus being programmed to execute the steps of: a) measuring an intensity profile of an image region corresponding to a potentially mitotic figure, and b) counting the image region as indicating a mitotic figure if its profile has a value greater than a prearranged threshold at a position in the profile having intensity associated with mitotic figure imagery".

These key features in combination with the other features of the claimed invention are neither taught nor suggested by (Vaisberg and Sundbland) prior art of record.

Conclusion

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Seyed Azarian whose telephone number is (571) 272-7443. The examiner can normally be reached on Monday through Thursday from 6:00 a.m. to 7:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mehta Bhavesh, can be reached at (571) 272-7453. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR.
Status information about the PAIR system, see http:// pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Seyed Azarian/
Primary Examiner, Art Unit 2624
Group Art Unit 2624
December 8, 2008